

What is claimed is:

1. A method for sequencing DNA by detecting the identity of a dideoxynucleotide incorporated to the 3' end of a DNA sequencing fragment using mass spectrometry, which comprises:
  - (a) attaching a chemical moiety via a linker to a dideoxynucleotide to produce a labeled dideoxynucleotide;
  - (b) terminating a DNA sequencing reaction with the labeled dideoxynucleotide to generate a labeled DNA sequencing fragment, wherein the DNA sequencing fragment has a 3' end and the chemical moiety is attached via the linker to the 3' end of the DNA sequencing fragment;
  - (c) capturing the labeled DNA sequencing fragment on a surface coated with a compound that specifically interacts with the chemical moiety attached via the linker to the DNA sequencing fragment, thereby capturing the DNA sequencing fragment;
  - (d) washing the surface to remove any non-bound component;
  - (e) freeing the DNA sequencing fragment from the surface; and
  - (f) analyzing the DNA sequencing fragment using mass spectrometry so as to sequence the DNA.
2. A method for sequencing DNA by detecting the identity of a plurality of dideoxynucleotides incorporated to the 3' end of different DNA

sequencing fragments using mass spectrometry, which comprises:

- (a) attaching a chemical moiety via a linker to a plurality of different dideoxynucleotides to produce labeled dideoxynucleotides;
- (b) terminating a DNA sequencing reaction with the labeled dideoxynucleotides to generate labeled DNA sequencing fragments, wherein the DNA sequencing fragments have a 3' end and the chemical moiety is attached via the linker to the 3' end of the DNA sequencing fragments;
- (c) capturing the labeled DNA sequencing fragments on a surface coated with a compound that specifically interacts with the chemical moiety attached via the linker to the DNA sequencing fragments, thereby capturing the DNA sequencing fragments;
- (d) washing the surface to remove any non-bound component;
- (e) freeing the DNA sequencing fragments from the surface; and
- (f) analyzing the DNA sequencing fragments using mass spectrometry so as to sequence the DNA.

3. The method of claim 2, wherein the chemical moiety is attached via a different linker to different dideoxynucleotides.

4. The method of claim 1 or 2, wherein the interaction between the chemical moiety attached via the linker to the DNA sequencing fragment

*Subj*

and the compound on the surface comprises a biotin-streptavidin interaction, a phenylboronic acid-salicylhydroxamic acid interaction, or an antigen-antibody interaction.

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Sub B1

5. The method of claim 1 or 2, wherein the step of freeing the DNA sequencing fragment from the surface comprises disrupting the interaction between the chemical moiety attached via the linker to the DNA sequencing fragment and the compound on the surface.

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6. The method of claim 5, wherein the interaction is disrupted by a means selected from the group consisting of one or more of a physical means, a chemical means, a physical chemical means, heat, and light.

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7. The method of claim 1 or 2, wherein the dideoxynucleotide comprises a cytosine or a thymine with a 5-position, or an adenine or a guanine with a 7-position, and the linker is attached to the 5-position of cytosine or thymine or to the 7-position of adenine or guanine.

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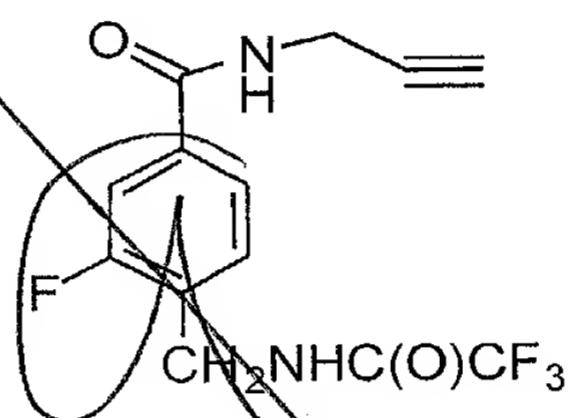
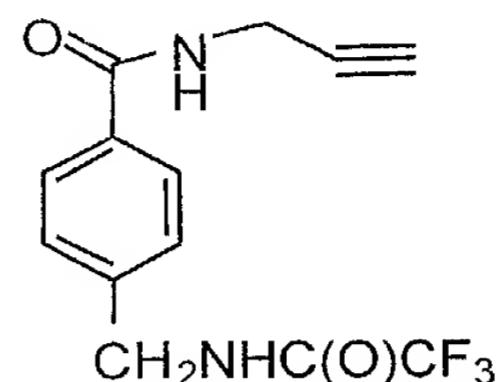
8. The method of claim 1 or 2, wherein the step of freeing the DNA sequencing fragment from the surface comprises cleaving the linker.

9. The method of claim 8, where the linker is cleaved by a means selected from the group consisting of one or more of a physical means, a

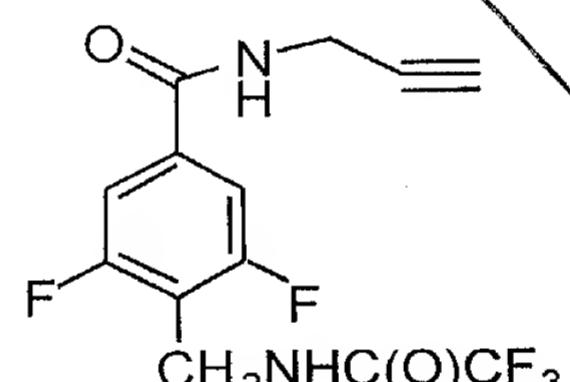
chemical means, a physical chemical means, heat,  
and light.

- 5                    10. The method of claim 9, wherein the linker is  
cleaved by ultraviolet light.
- Sub B3  
10                    11. The method of claim 1 or 2, wherein the linker  
comprises a derivative of 4-aminomethyl benzoic  
acid.
12. The method of claim 11, wherein the linker  
comprises one or more fluorine atoms.

13. The method of claim 12, wherein the linker is selected from the group consisting of:



and



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14. The method of claim 1, wherein a plurality of different labeled dideoxynucleotides is used to generate a plurality of different labeled DNA sequencing fragments.

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15. The method of claim 3 or 14, wherein a plurality of different linkers is used to increase mass separation between different labeled DNA sequencing fragments and thereby increase mass spectrometry resolution.

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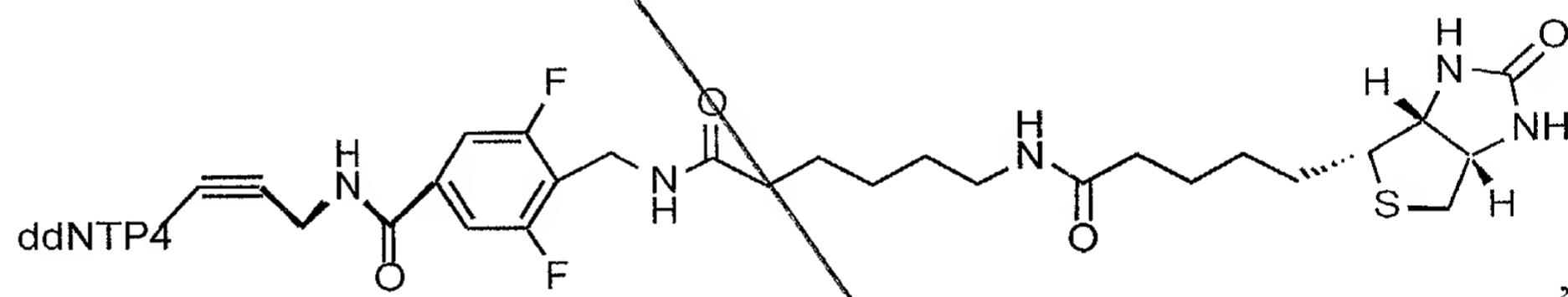
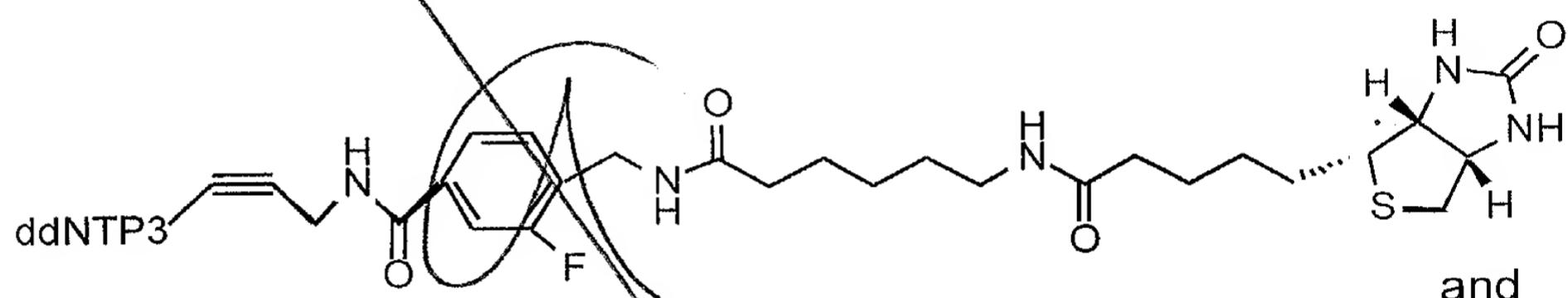
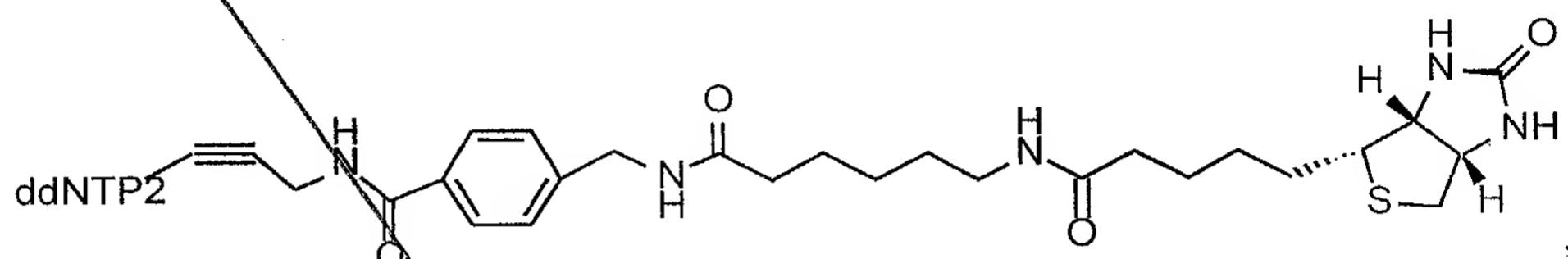
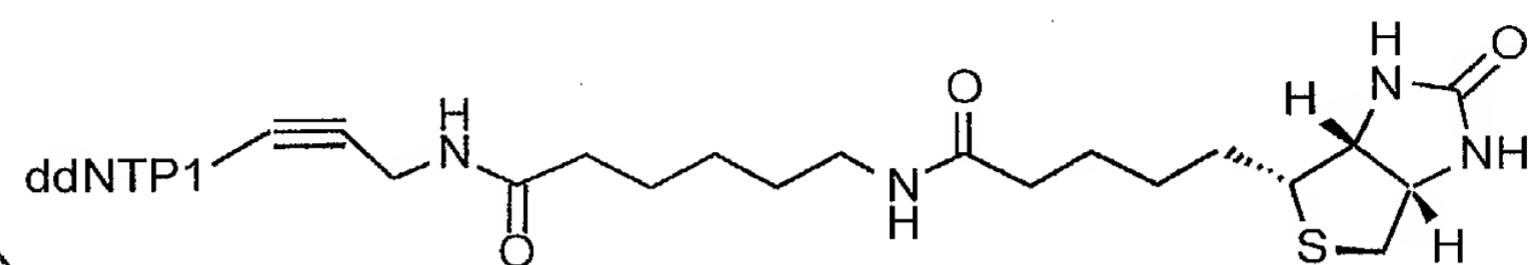
16. The method of claim 1 or 2, wherein the chemical moiety comprises biotin, the labeled dideoxynucleotide is a biotinylated dideoxynucleotide, the labeled DNA sequencing fragment is a biotinylated DNA sequencing fragment, and the surface is a streptavidin-coated solid surface.

17. The method of claim 16, wherein the biotinylated dideoxynucleotide is selected from the group consisting of ddATP-11-biotin, ddCTP-11-biotin, ddGTP-11-biotin, and ddTTP-16-biotin.

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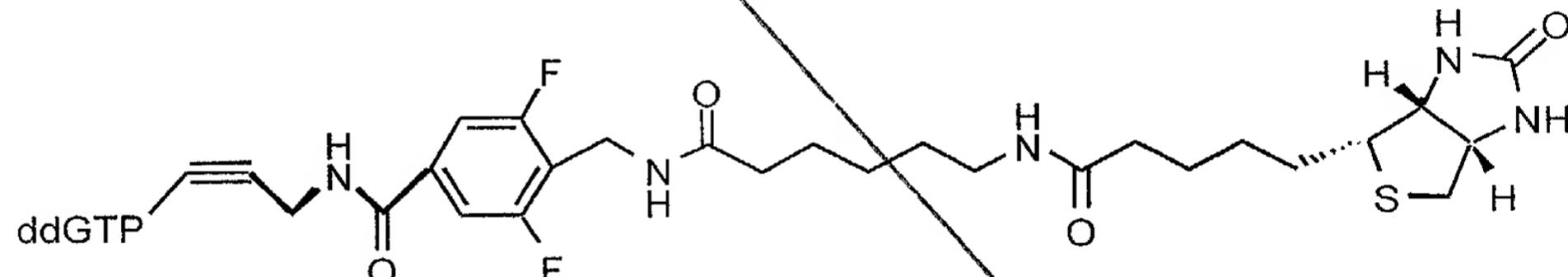
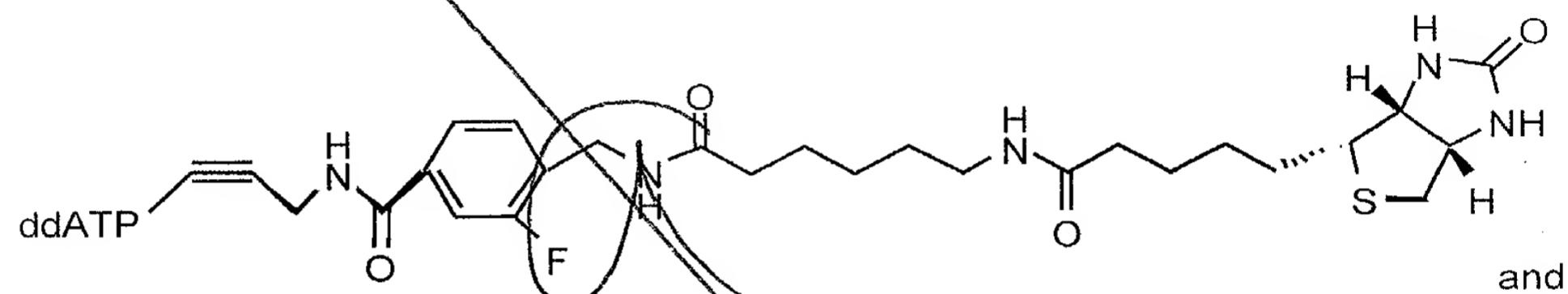
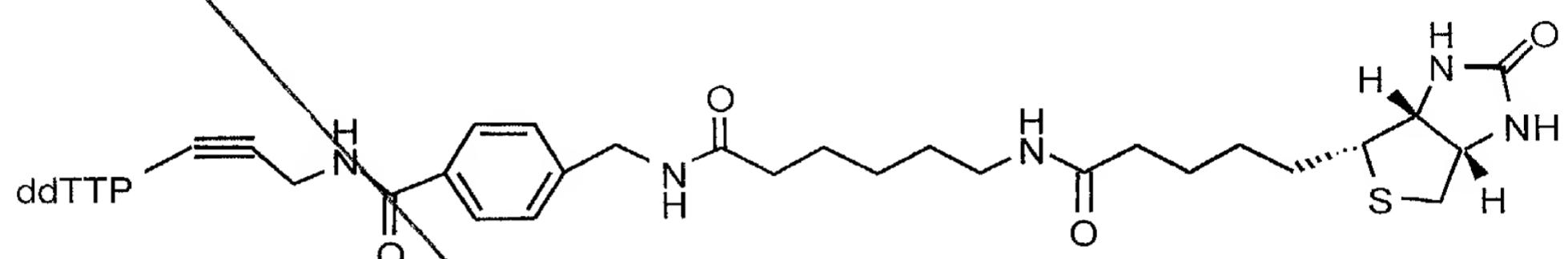
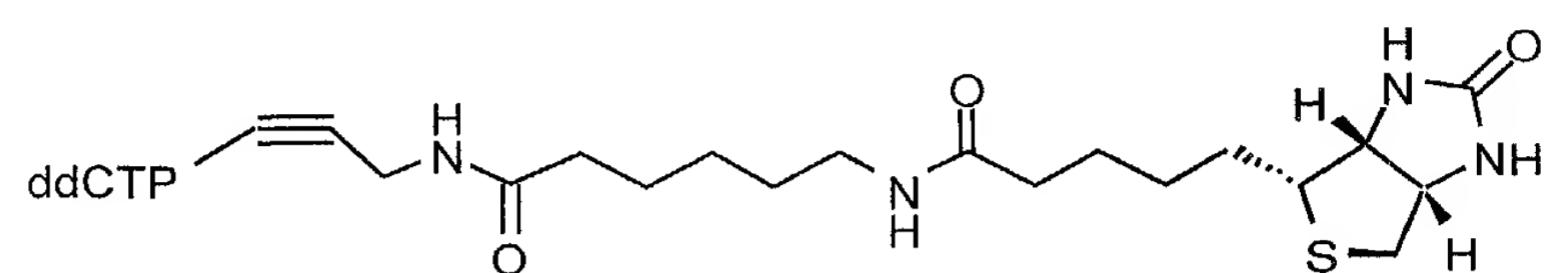
18. The method of claim 16, wherein the biotinylated dideoxynucleotide is selected from the group consisting of:

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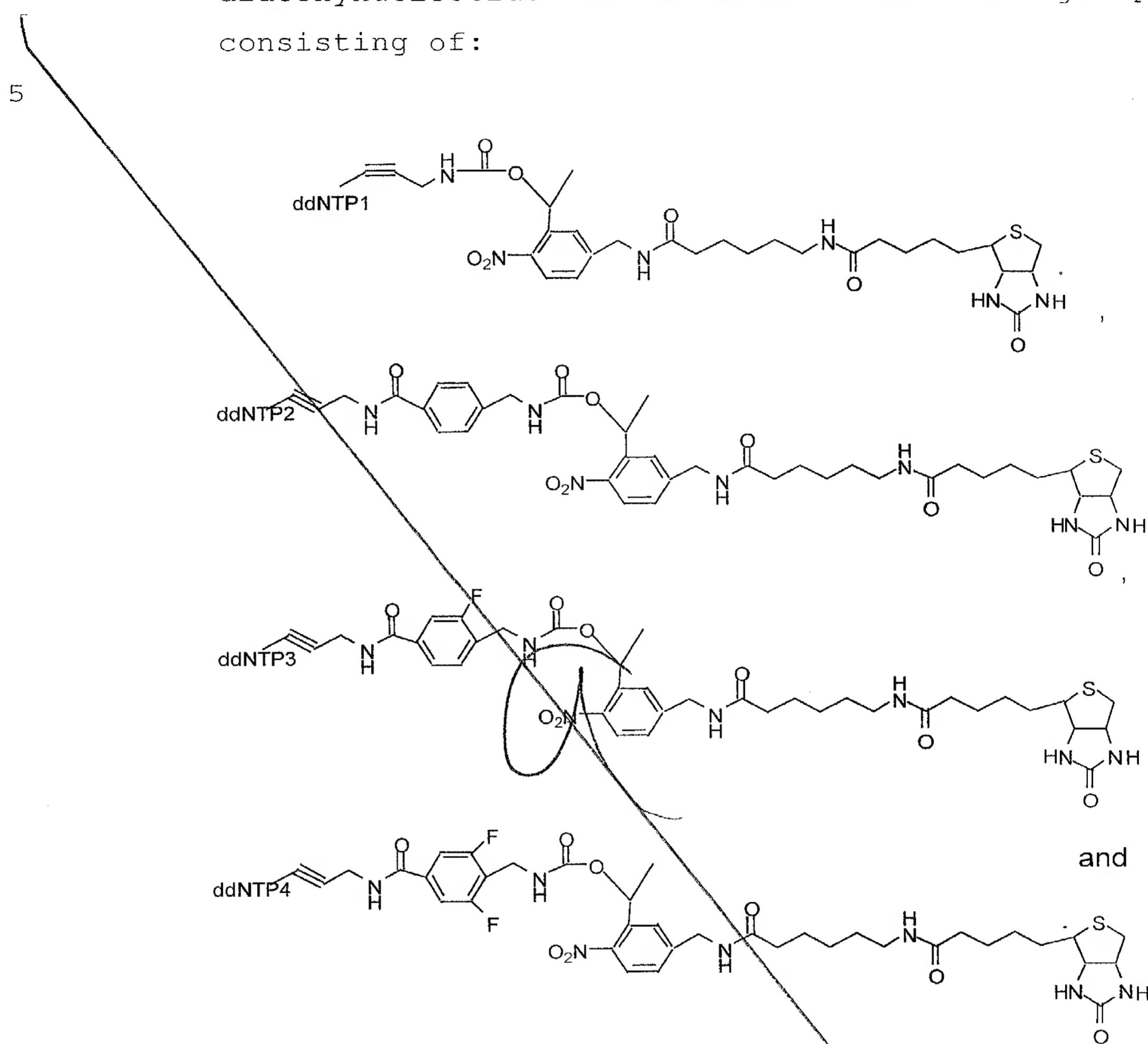


wherein ddNTP1, ddNTP2, ddNTP3, and ddNTP4 represent four different dideoxynucleotides.

19. The method of claim 18, wherein the biotinylated dideoxynucleotide is selected from the group consisting of:

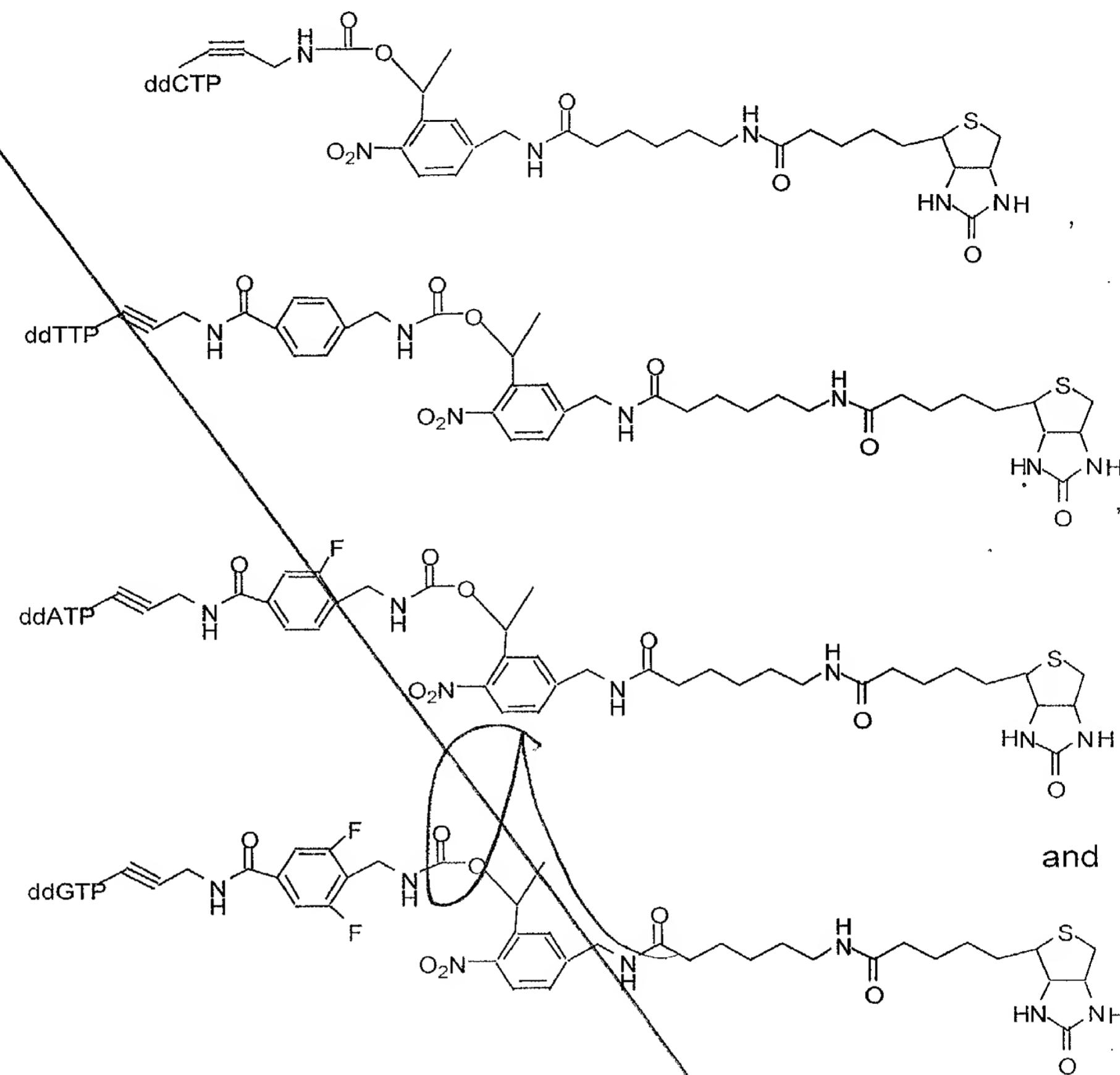


20. The method of claim 16, wherein the biotinylated dideoxynucleotide is selected from the group consisting of:



wherein ddNTP1, ddNTP2, ddNTP3, and ddNTP4 represent four different dideoxynucleotides.

21. The method of claim 20, wherein the biotinylated dideoxynucleotide is selected from the group consisting of:

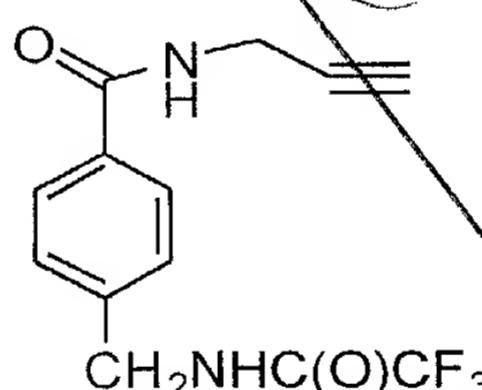
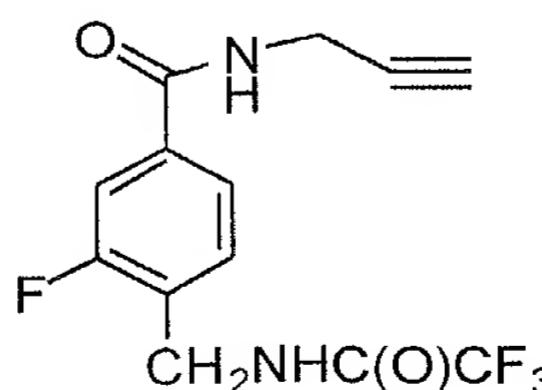


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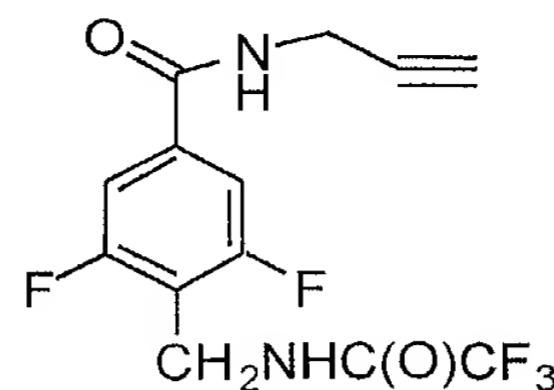
22. The method of claim 16, wherein the streptavidin-coated solid surface is a streptavidin-coated magnetic bead or a streptavidin-coated silica glass.

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23. The method of claim 1 or 2, wherein steps (b) to (e) are performed in a single container or in a plurality of connected containers.

24. Use of the method of claim 1 or 2 for detection of single nucleotide polymorphisms, genetic mutation analysis, serial analysis of gene expression, gene expression analysis, identification in forensics, genetic disease association studies, genomic sequencing, translational analysis, or transcriptional analysis.
- 10 25. A linker for attaching a chemical moiety to a dideoxynucleotide, wherein the linker comprises a derivative of 4-aminomethyl benzoic acid.
- 15 26. The linker of claim 25, wherein the linker comprises one or more fluorine atoms.
- 20 27. The linker of claim 26, wherein the linker is selected from the group consisting of:
- 25 
- 30 

and

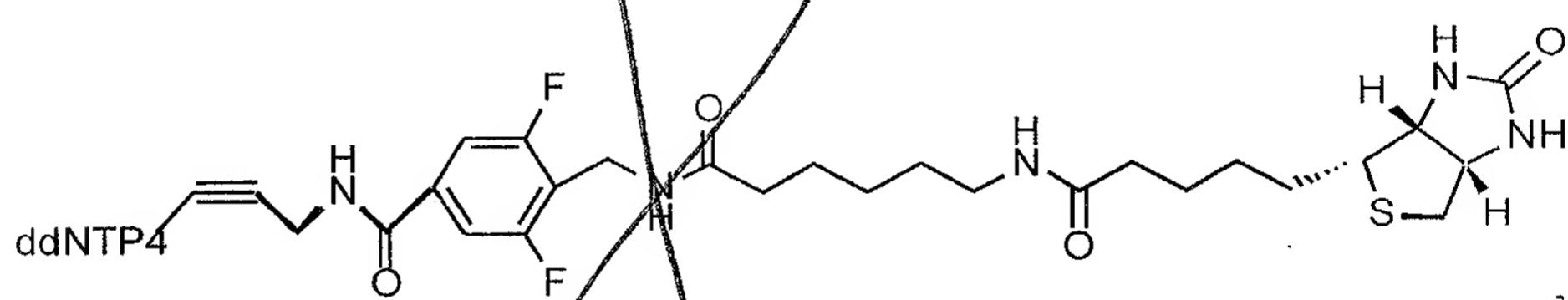
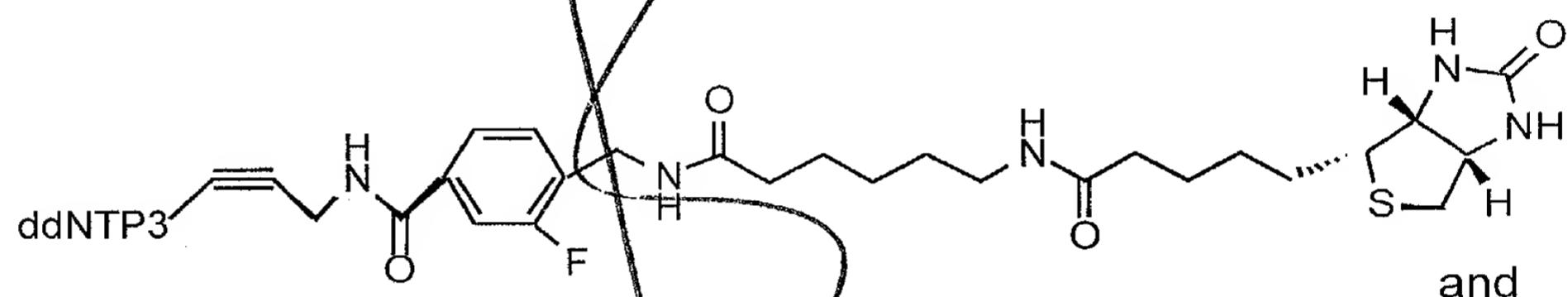
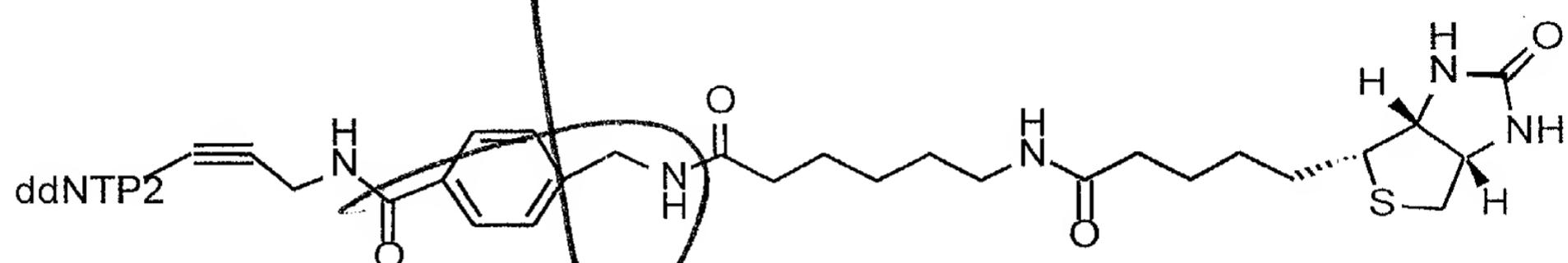
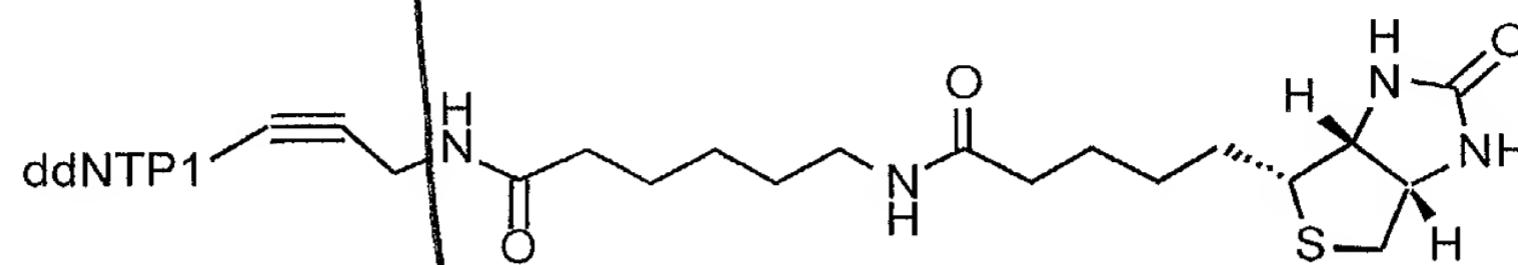


- 5        28. The linker of claim 25, wherein the linker is cleavable by a means selected from the group consisting of one or more of a physical means, a chemical means, a physical chemical means, heat, and light.
- 10        29. The linker of claim 28, wherein the linker is cleavable by ultraviolet light.
- 15        30. The linker of claim 25, wherein the chemical moiety comprises biotin, streptavidin, phenylboronic acid, salicylhydroxamic acid, an antibody, or an antigen.
- 20        31. The linker of claim 25, wherein the dideoxynucleotide comprises a cytosine or a thymine with a 5-position, or an adenine or a guanine with a 7-position, and the linker is attached to the 5-position of cytosine or thymine or to the 7-position of adenine or guanine.
- 25        32. Use of the linker of claim 25 in DNA sequencing using mass spectrometry, wherein the linker increases mass separation between different

dideoxynucleotides and increases mass spectrometry resolution.

- 5           33. A labeled dideoxynucleotide, which comprises a chemical moiety attached via a linker to a 5-position of cytosine or thymine or to a 7-position of adenine or guanine.
- 10          34. The labeled dideoxynucleotide of claim 33, wherein the linker is cleavable by a means selected from the group consisting of one or more of a physical means, a chemical means, a physical chemical means, heat, and light.
- 15          35. The labeled dideoxynucleotide of claim 34, wherein the linker is cleavable by ultraviolet light.
- 20          36. The labeled dideoxynucleotide of claim 33, wherein the chemical moiety comprises biotin, streptavidin, phenylboronic acid, salicylhydroxamic acid, an antibody, or an antigen.

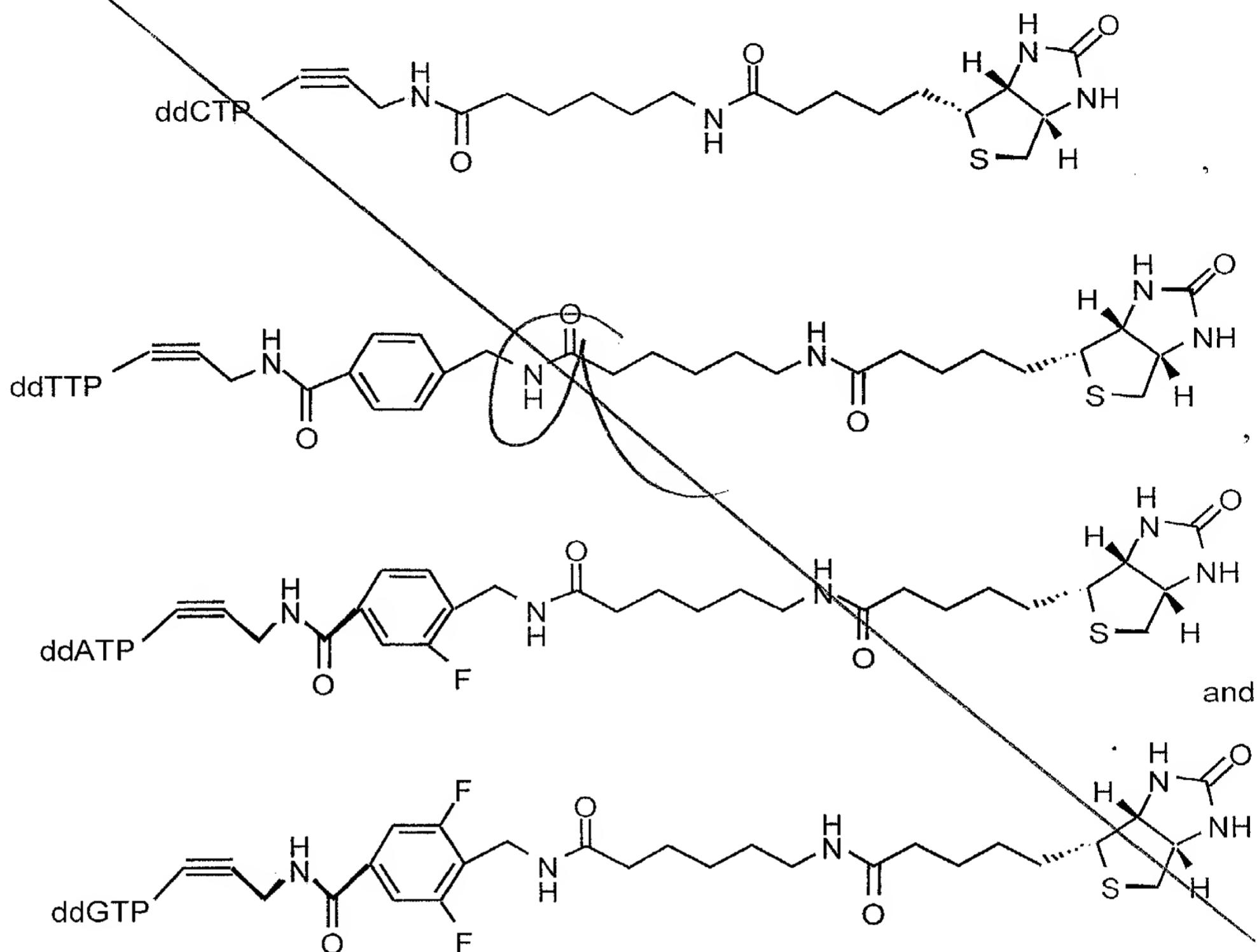
37. The labeled dideoxynucleotide of claim 33,  
wherein the labeled dideoxynucleotide is  
selected from the group consisting of:



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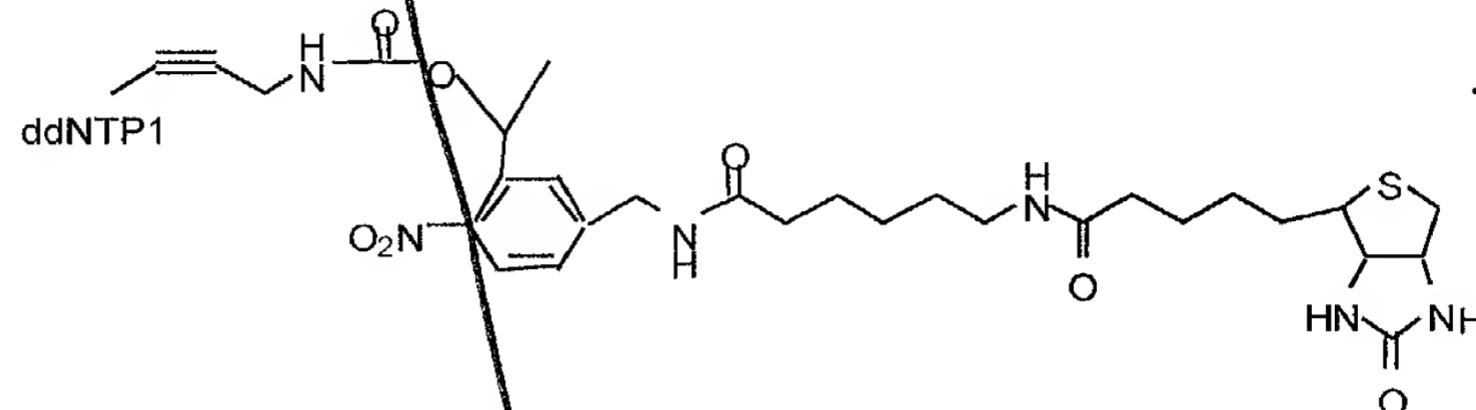
wherein ddNTP1, ddNTP2, ddNTP3, and ddNTP4  
represent four different dideoxynucleotides.

38. The labeled dideoxynucleotide of claim 37,  
wherein the labeled dideoxynucleotide is  
selected from the group consisting of:

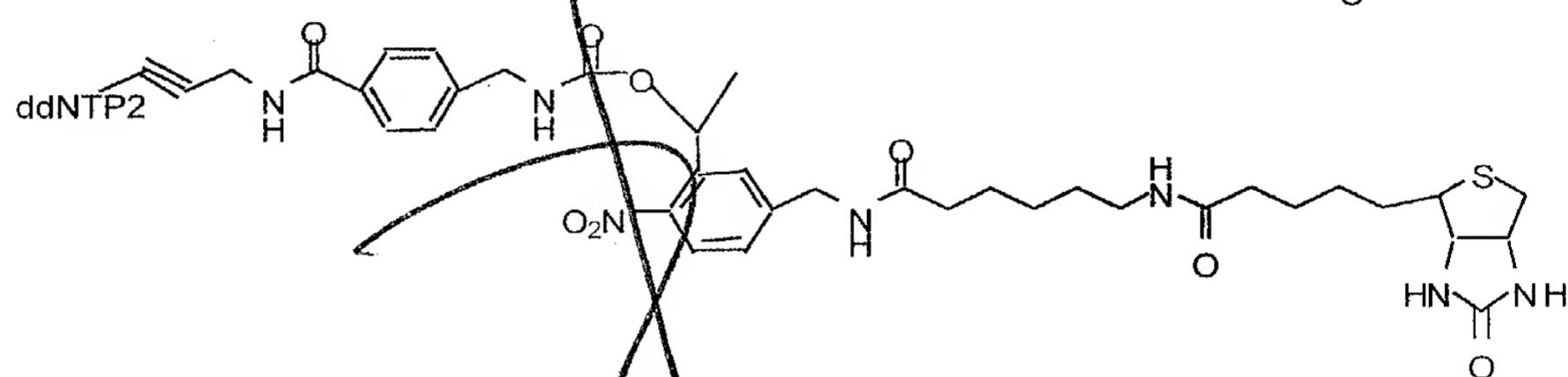


39. The labeled dideoxynucleotide of claim 33,  
wherein the labeled dideoxynucleotide is  
selected from the group consisting of:

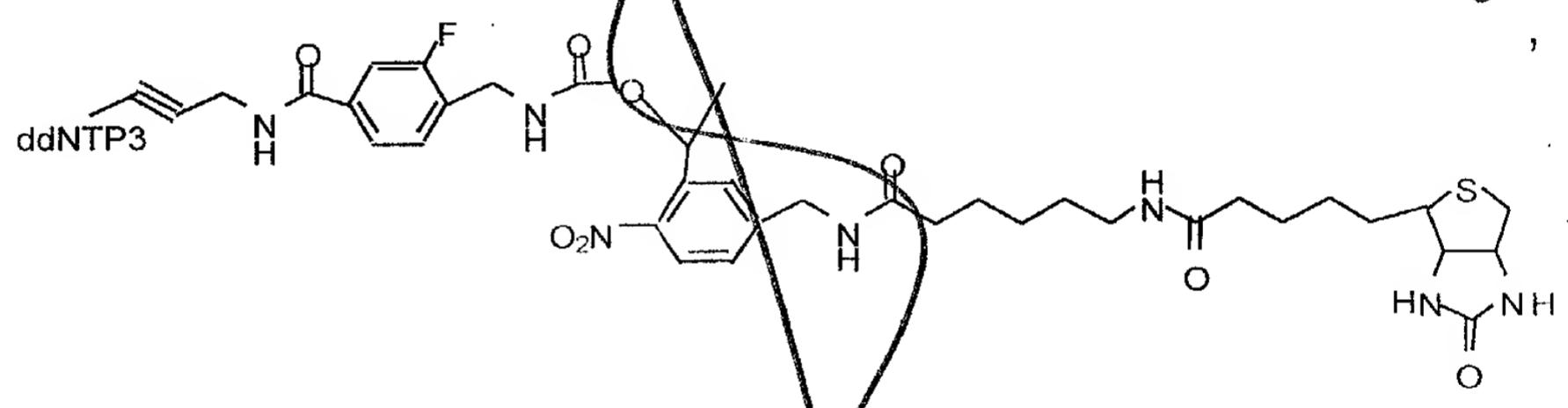
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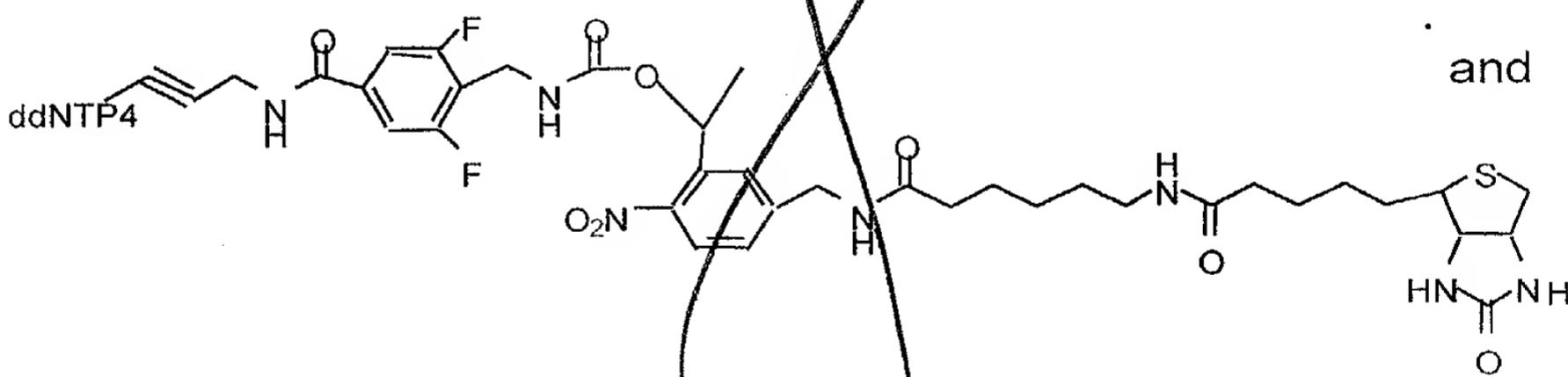
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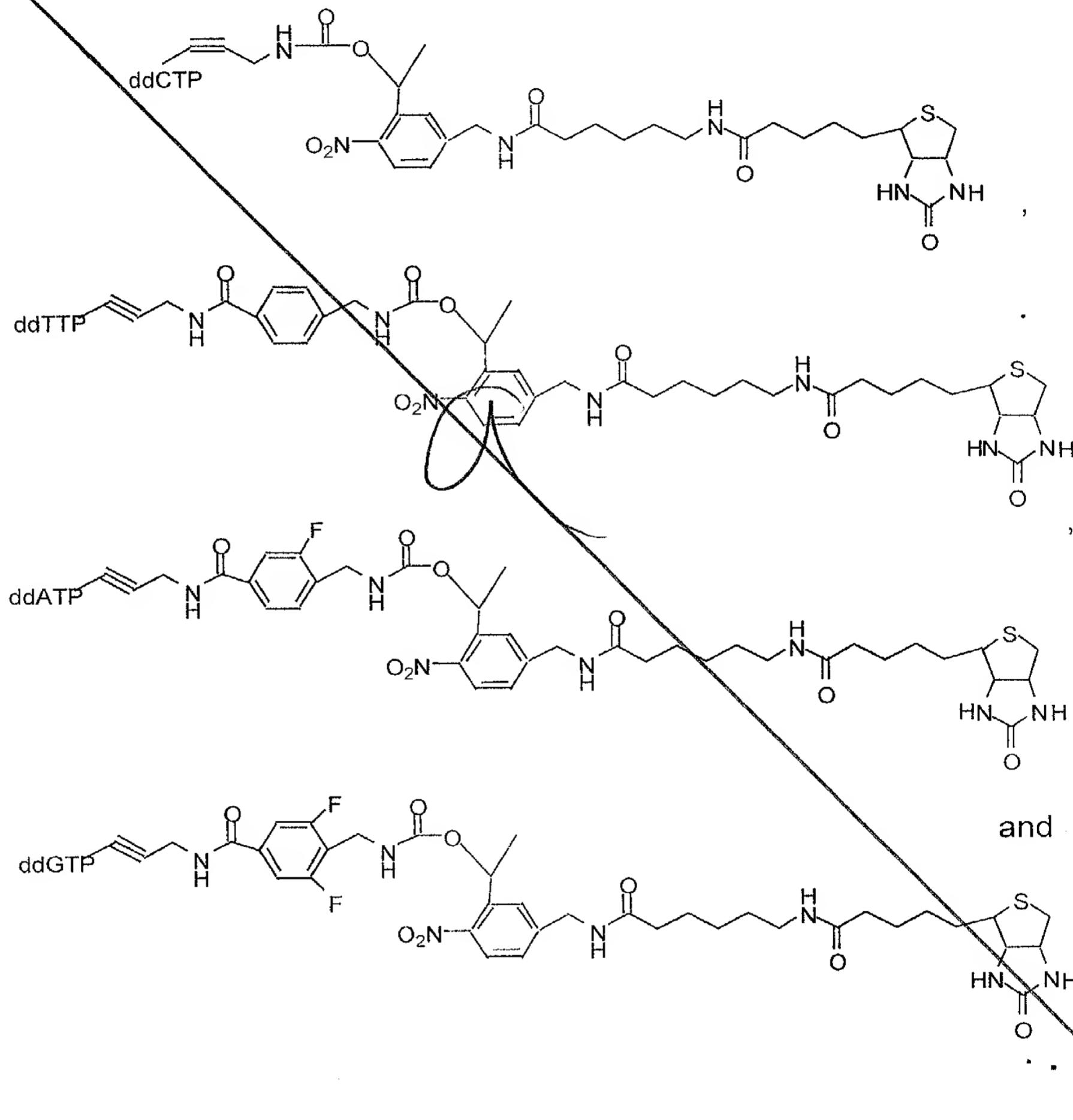


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wherein ddNTP1, ddNTP2, ddNTP3, and ddNTP4 represent four different dideoxynucleotides.

40. The labeled dideoxynucleotide of claim 39, wherein the labeled dideoxynucleotide is selected from the group consisting of:



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41. Use of the labeled dideoxynucleotide of claim 33  
in DNA sequencing using mass spectrometry,  
wherein the linker increases mass separation  
between different labeled dideoxynucleotides and  
increases mass spectrometry resolution.

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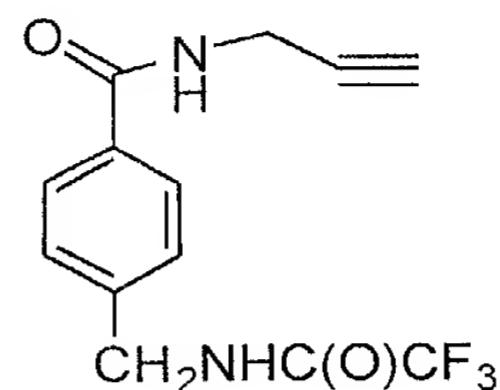
42. A system for separating a chemical moiety from other components in a sample in solution, which comprises:
- (a) a channel coated with a compound that specifically interacts with the chemical moiety, wherein the channel comprises a plurality of ends;
- (b) a plurality of wells each suitable for holding the sample;
- (c) a connection between each end of the channel and a well; and
- (d) a means for moving the sample through the channel between wells.
43. The system of claim 42, wherein the interaction between the chemical moiety and the compound coating the surface is a biotin-streptavidin interaction, a phenylboronic acid-salicylhydroxamic acid interaction, or an antigen-antibody interaction.
44. The system of claim 42, wherein the chemical moiety is a biotinylated moiety and the channel is a streptavidin-coated silica glass channel.
45. The system of claim 44, wherein the biotinylated moiety is a biotinylated DNA sequencing fragment.
46. The system of claim 42, wherein the chemical moiety can be freed from the surface by disrupting the interaction between the chemical moiety and the compound coating the surface.

47. The system of claim 46, where the interaction  
can be disrupted by a means selected from the  
group consisting of one or more of a physical  
means, a chemical means, a physical chemical  
means, heat, and light.
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48. The system of claim 42, wherein the chemical  
moiety is attached via a linker to another  
chemical compound.
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49. The system of claim 48, wherein the other  
chemical compound is a DNA sequencing fragment.
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50. The system of claim 48, where the linker is  
cleavable by a means selected from the group  
consisting of one or more of a physical means, a  
chemical means, a physical chemical means, heat,  
and light.
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51. The system of claim 50, wherein the channel is  
transparent to ultraviolet light and the linker  
is cleavable by ultraviolet light.
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52. A multi-channel system, which comprises a  
plurality of the system of claim 42.
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53. The multi-channel system of claim 52, wherein  
the channels are in a chip.
54. The multi-channel system of claim 53, which  
comprises 96 channels in a chip.

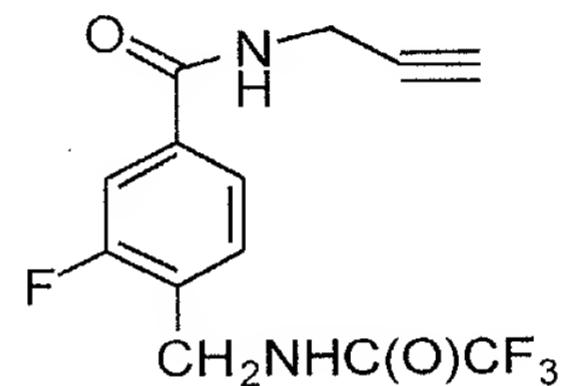
55. Use of the system of claim 42 or 52 for separating one or more DNA sequencing fragments, wherein each fragment is terminated with a dideoxynucleotide attached via a linker to the chemical moiety.
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56. A method of increasing mass spectrometry resolution between different DNA sequencing fragments, which comprises attaching different linkers to different dideoxynucleotides used to terminate a DNA sequencing reaction and generate different DNA sequencing fragments, wherein the different linkers increase mass separation between the different DNA sequencing fragments, thereby increasing mass spectrometry resolution.
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57. The method of claim 56, wherein one or more of the different linkers comprises one or more fluorine atoms.

58. The method of claim 57, wherein one or more of the different linkers is selected from the group consisting of:

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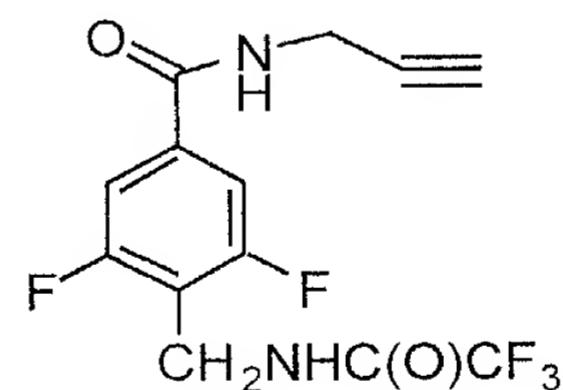


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and



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